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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/832,865 | 04/12/2001 | Hua Yu | USF-T142X | 1377 |
| 23567 | 7590 | 03/25/2005 | EXAMINER | |
| ELDEN R SODOWSKY P O BOX 223234 CHANTILLY, VA 20153 | | | GAMBEL, PHILLIP | |
| | | ART UNIT | | PAPER NUMBER |
| | | 1644 | | |

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-----------------|--------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/832,865 | YU, HUA |
| | Examiner | Art Unit |
| | Phillip Gambel | 1644 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 09 January 2005.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-9 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-9 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment, filed 10/12/04, has been entered.

Claim 1 has been amended.

Claims 10-15 have been canceled.

Claims 1-9 are pending.

Claims 1-9 as they read on the elected species of tumor cells and the combination of GM-CSF and IL-12

2. Upon reconsideration of applicant's amended claims, filed 12/12/04, in conjunction with the arguments that the claimed subject matter is drawn to cells of the method which are engineered to express soluble CD40 and not membrane bound CD40, the previous rejection under 35 USC 102(e) as being anticipated by Hoo et al. (U.S. Patent No. 6,482,407), has been withdrawn.

3. Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite in that it lacks proper antecedent basis for "said tumor cells".

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dranoff et al. (U.S. Patent No. 5,904,920) (1449; #B) in view of Heath et al. (WO 94/04570) (1449; #H) and Levitsky et al. (J. Immunol. 156: 3858-3865 (1996)).

Dranoff et al. teach methods of regulating immune response utilizing cytokines and antigens, including the transfection and administration of tumor cells transfected with cytokines such as GM-CSF and IL-12 (e.g., see Summary of the Invention; Detailed Description of the Invention, including column 6, paragraph 2; column 8, paragraphs 4-6), wherein said tumor cells are rendered proliferation incompetent, including the use of irradiation (e.g. column 8, paragraph 2) (see entire document, including Detailed Description of the Invention).

Dranoff et al. differs from the claimed methods by not including soluble CD40 in the transfection of tumor cells to increase immune responses and by not teaching B cell lymphomas as a target for treatment with CD40 as well as GM-CSF and IL-12.

Levitsky et al. teach GM-CSF transduced tumor cell-based vaccinations for B cell lymphomas (see entire document, including Abstract). Levitsky et al. teach the effectiveness of the paracrine production of cytokines by tumor cells in the generation of effective immune responses (see Discussion).

Heath et al. teach that CD40⁺ malignancies such as B cell lymphomas are sensitive to inhibition via soluble CD40 (see entire document, including page 3, paragraph 3 and page 21, paragraph 1). Heath et al. further teach the recombinant production of soluble CD40, including introducing CD40 by an expression vector into host cells (see Soluble CD40 Molecules on pages 6-13)

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Heath et al. to those of Dranoff et al. by including the transfection of soluble CD40 into tumor cells, particularly CD40⁺ malignancies such as B cell lymphomas, to increase the effectiveness of tumor-based vaccination regimens, by taking advantage of the paracrine functions of GM-CSF and IL-12 in generating appropriate anti-tumor responses, and by taking advantage of the sensitivity of said CD40⁺ malignancies to soluble CD40.

Accordingly, one of ordinary skill in the art at the time the invention was made would have been motivated to transfet CD40⁺ tumor cells, such as B cell lymphoma with those cytokines (e.g. GM-CSF and IL-12) that stimulate the appropriate anti-tumor responses along with the appropriate agent that specifically inhibits CD40:CD40 ligand interactions and signaling in said tumor cells to increase the efficacy of tumor cell vaccinations by addressing different targets by increasing host immune responses while decreasing stimulatory signals to said CD40⁺ malignancies, wherein said combination regimens were consistent with practices known at the time the invention was made, as evidenced by Dranoff et al.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. No claim allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gabel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
March 21, 2005

